

Attorney Docket No.: PTQ-0027
Inventors: Van Eyk et al.
Serial No.: 09/115,589
Filing Date: July 15, 1998
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Amendments to the Specification:

Please replace the paragraph beginning at page 10, line 21 with the following:

The phrase "myofilament protein modification product(s)" is intended to include one or more modification products of a myofilament protein associated with damage to the myocardium or skeletal muscle. For example, a myofilament protein modification product can be a modified form of the protein or a peptide fragment of a myofilament protein such as α -actinin, a troponin (e.g., troponin I, troponin T), or myosin light chain 1. Examples of such peptide fragments include all or a portion of the carboxyl-terminal region consisting of amino acids 194-210 (rat sequence, see Figure 17B, SEQ ID NO:26; corresponding human sequence, see Figure 17A, SEQ ID NO:27) of troponin I, or all or a portion of the amino-terminal region consisting of amino acids 1 to 193 of troponin I (rat sequence, SEQ ID NO:20; corresponding human sequence, SEQ ID NO:21) (referring to the sequence published in any one of Vallins et al. 1990, FEBS Lett. 270:57-61; Armour et al. 1993, Gene, 131:287-292; or Hunkeler et al. 1991, Circ. Res. 69:1409-14). Alternatively, a myofilament protein modification product can be a peptide fragment of

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myosin light chain 1, such as all or a portion of all the carboxyl-terminal region consisting of amino acids 20 to ~~192~~ 199 (SEQ ID NO:28) of myosin light chain 1, or all or a portion of the amino-terminal region consisting of amino acids 1 to 19 (SEQ ID NO:29) of myosin light chain 1 (referring to the sequence published in Swiss-Prot P16409; also see Swiss-Prot:P08590 set forth herein in SEQ ID NO:50 and published by Kurabayashi et al. J. Biol. Chem. 1988 263:13930 referred to in Zimmermann et al. 1990, J. Mol. Biol. 211(3):505-513). A myofilament protein modification product can be a covalent or non-covalent complex of two or more intact proteins or fragments of proteins, such as α -actinin, troponin I, T, or C, or myosin light chain 1, or covalent or non-covalent complexes of these proteins or fragments thereof with other proteins or fragments thereof. A myofilament protein modification product can also be such a complex of peptide fragments of two or more of α -actinin, troponin I, T or C, or myosin light chain 1, or such complexes of these proteins with other proteins or fragments thereof. Such complexes include those formed from any combination of the three troponins (troponin I, T and C), or fragments thereof such as, for example: TnI (amino acids 1 to 193; rat sequence, SEQ ID NO:20; corresponding human

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sequence, SEQ ID NO:21) with TnT (amino acids 191-298; rat sequence, SEQ ID NO:30; corresponding human sequence, SEQ ID NO:32); and TnI (amino acids 1 to 193; rat sequence, SEQ ID NO:20; corresponding human sequence, SEQ ID NO:21) with TnC (SEQ ID NO:48) (amino acids 1 to 94 (SEQ ID NO:49) (see Table 4).

Please replace the paragraph beginning at page 12, line 14, with the following:

The terms "severe ischemia" and "severe ischemia/reperfusion injury" refer to situations where irreversible damage to skeletal muscle or the myocardium has occurred, i.e., situations where the muscle cannot regain its full ability to contract. Usually, in such situations, there is a loss of cellular membrane integrity and cellular proteins are released and necrosis occurs. Severe myocardial ischemia and/or ischemia/reperfusion injury are often marked by the presence of one or more of a myosin light chain 1 modification product(s) (e.g., amino acid residues 20 to ~~192~~ 199 (SEQ ID NO:28)), an additional TnI modification product(s) (e.g., amino acid residues 63 to 193; rat sequence, SEQ ID NO:22; corresponding human sequence, SEQ ID NO:23, amino acid residues 73 to 193; rat sequence, SEQ ID NO:24; corresponding human sequence, SEQ ID

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NO:25), TnT modification product(s), and α -actinin
modification product(s).

Please replace the paragraph beginning at page 14, line
3, with the following:

Assessment of myocardial or skeletal muscle damage in a
biological sample can be performed by direct detection of
myofilament protein modification product(s) in the sample,
using, for example, chromatography techniques such as HPLC,
or electrophoresis. These analyses are used to detect
differences between elution profiles of samples obtained
before and after, for example, treatment of hypoxemia,
hypoxia, ischemia or ischemia/reperfusion. As well, the
appearance or disappearance of one or more myofilament
protein modification products, peptides, or fragments, such
as, for example, cardiac TnI residues 194 to 210 (rat
sequence, SEQ ID NO:26; corresponding human sequence, SEQ ID
NO:27) or myosin light chain residues 1 to ~~192~~ 199 (rat
sequence, SEQ ID NO:28; also see Swiss-Prot:P08590 provided
herein as SEQ ID NO:50 and published by Kurabayashi et al.
J. Biol. Chem. 1988 263:13930 referred to in Zimmermann et
al. 1990, J. Mol. Biol. 211(3):505-513), in the elution
profiles obtained during HPLC analysis can be used as
indicators of muscle damage.